ADC predicted poor histologic tumor response (TRG3-5 versus TRG1-2) with 91% sensitivity and 83% specificity (area under curve (AUC)=0.89, 95% confidence interval (CI)=0.74-1.0, p<0.001). Using the 30th percentile, an increase in ADC predicted poor PFS with 89% sensitivity and 71% specificity (AUC=0.75, 95% CI=0.54-0.95, p=0.051). Univariate regression analysis also revealed that the ADC increase was significantly associated to poor PFS (hazard ratio=9.7, 95% CI=1.21-78.30, p=0.033).

Conclusion: By ADC histogram analysis of DWMRI acquired during NACT of LARC we identified low histogram percentiles as predictive of histologic tumor response in particular, but also long-term survival. The results require validation in larger, independent cohorts, but are promising for identification of patients that may benefit from individualized treatment approaches for improved disease outcome.

PO-0926
Simulation of FMISO diffusion-retention in a three-dimensional tumor model
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Purpose or Objective: Tumor hypoxia is prognostic for poor outcome after radiotherapy (RT). A method for non-invasive assessment of hypoxia is PET using hypoxia radiotracers such as FMISO. The goal of this study was to develop and evaluate a tool to simulate 3D oxygen distribution and the resulting FMISO accumulation on realistic vessel architectures, which can be compared to measured PET activities in small animal experiments.

Material and Methods: Two FaDu tumors (human HNSCC) were grown on the right hind leg of nude mice. Imaging was performed after a growth phase of about 5 weeks. FMISO was injected into the tail vein of the anesthetized mice with an activity of ~12MBo for dynamic PET/MRI. ROIs inside the left ventricle and in the tumor were chosen to determine blood and tumor time activity curves (TACs). After image acquisition tumors were excised, snap frozen and cut into consecutive sections (20µm). Sections were stained with immunofluorescence-labeled antibodies for endothelial marker CD31 and scanned with a Zeiss Axioplan 2 fluorescence microscope. Obtained immunofluorescence images were rigidly registered, manually adjusted and thresholded to create a binary 3D vessel map. These maps were used to simulate 3D oxygen distributions based on a Michaelis-Menten relation. Using the oxygen distribution and the dynamic activity in the left ventricle as input, FMISO retention was simulated on the same vessel maps. A tumor ROI was selected and its average activity at different time points post-injection (p.i.) compared against the measured activity in the same region on the PET scan (tumor TAC).

Results: 02 histograms showed a large difference between 2D and 3D simulations, with much lower values for 2D simulations than for 3D (5.94 mmHg vs 26.57 mmHg). Mean values were closer together (8.9 mmHg vs 13.2 mmHg). This is due to the large amount of anoxic voxels (pO2 < 1 mmHg) in the 2D simulation, which made up 17.5% of all simulated voxels in 2d, but less than 1% in the 3D simulations (see Table 1). Visually, the 3D simulations result in a TAC with a similar overall shape compared to the TAC measured with small animal PET, but with a 20.7% overestimation of activity. However, the 2D simulations severely overestimated the total activity by 99.2% (2D) when compared against measured activity in the tumor after 90min as determined by PET.

Conclusion: 3D simulations based on real 3D vessel architecture is feasible. Our FMISO simulations showed large discrepancies between 2D and 3D simulation approaches, with the 3D values being closer to the PET measurements. Verification of 3D tracer accumulation patterns in additional tumors against pimonidazole stainings is still necessary to validate and calibrate the method, with PET scans in the same test subject to confirm observed activity.

PO-0926
Voxel-based PSMA-PET/histopathology analysis in patients with primary prostate cancer
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Purpose or Objective: Tumorcontrol of primary prostate cancer (PC) is dose dependent. Dominant index lesions (DIL) within the prostatic gland are responsible for local and distant failure. Radionuclide-labelled inhibitors of prostate-specific membrane antigen (PSMA-PET) showed promising preclinical and clinical results in detection of primary prostate cancer. We correlated PET/histopathology using a new coregistration approach, which allows pixel-wise evaluation of the tracers performance in prostatic tissue. Aim of this work is to evaluate the diagnostic accuracy of 68Ga-PSMA-PET/CT and to determine potential SUV-thresholds enabling a focal dose escalation on DIL delineated by PET.

Material and Methods: 10 patients with primary PC and 68Ga-PSMA-PET/CT were enrolled. After prostatectomy, thorough histopathological preparation and anatomical-based coregistration between in-vivo and ex-vivo material was performed. Simulated PET-images were generated out of blurred 3D histopathological tumor distribution (histoPET). The coregistration was further optimized by matching histoPET information with the in-vivo PET signal. The tracer performance was evaluated by coefficient of determination (R²) between histoPET/PSMA-PET patterns and SUV-values within different tissue types.

Results: 1 patient was excluded due to imprecise pathological preparation. Mean R² value was 60 % (± 15.2, range: 42.5-81.6). SUVmax of PSMA-PET was located in non resolution adapted / resolution adapted PC-tissue in 80%/90% of patients. Mean SUVmean in non resolution adapted PC and non-PC tissue was 6.1 (range: 2 - 21) and 2.7 (range: 1.3 - 8.2), respectively. The ratio between SUVmean in PC / non-PC was 2.2 (SD ± 0.6).
PO-0927

Bone texture analysis as predictive of bone radiation damage in patients undergoing pelvic RT.

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Purpose or Objective: To assess the potential role for a CT-based, bone texture analysis as a predictive factor of bone radiation damage in patients undergoing radiotherapy (RT) for pelvic malignancies.

Material and Methods: We performed a retrospective analysis of suitable patients treated with RT for pelvic malignancies from January 2010 to December 2014. The DICOM CT data acquired for RT planning were collected, and used for a homemade ImageJ macro analysis. Two region of interest (ROI) were selected: the L5 vertebral body and the femoral heads. Typical texture analysis (TA) parameters were retrospectively evaluated: mean (M), standard deviation (SD), skewness (SK), kurtosis (K), entropy (E) and uniformity (U).

The patients who developed bone RT-related damages (i.e.: pelvic bone stress fracture, radiation osteitis, insufficiency fractures) during the follow-up constitute the study patients (SP) group. The TA data were collected for a comparative analysis also in a control group of patients (CP): 2:1 ratio, with respect to SP) not developing bone damages. The CPs were matched taking into account: age, sex, type of tumor, intent of postoperative treatment, comparable doses to the considered organs-at-risk. As for the statistical comparisons, we performed a univariate analysis (Pearson correlation) and a multivariate analysis (logistic regression) using the SPSS software 17.0.

Results: Twenty-four SPs and 48 CPs are the subject of this report. Out of SPs, postoperative RT was delivered for cancer of the digestive tract (anal or rectal) in thirteen patients (54%); of the female reproductive organs (endometrial or cervical) in 9 (37%); and of the excretory apparatus (prostate or bladder) in 3 patients (9%). In the comparison between SP and CP groups, the univariate analysis showed a significant correlation of the ROI parameters of L5: SD (p=0.012); K (p=0.001), E (p=0.001); U (p=0.008), and of the femoral head: M (p=0.001); SD (p=0.001), with the development of bone damage. The logistic regression highlighted a significant correlation with the ROI parameters of L5: E (p=0.004); U (p=0.014), and femoral head M (p=0.022); and SD (p=0.042), with an Overall Model Nagelkerke R Square of 0.590.

Conclusion: These results (with the limit of a small series) and those reported in previous related studies deserve some interest, since the knowledge of predictive factors of bone radiation damage might help in patients’ selection for pelvic RT, and in identifying suitable dose constraints for the bony pelvis in RT planning for patients at risk.

PO-0928

Impact of fuzzy-thresholding of 18F-FDG PET images for cervical cancer recurrence prediction

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Purpose or Objective: In case of cervix cancer irradiation, parameters extracted from initial 18F-FDG-PET images can be used to predict recurrence. FDG PET parameters are classically computed among voxels binary selected in the segmentation step. We proposed the use of fuzzy-thresholding, providing tumor membership probability map, and present a generalization of the computation of FDG PET parameters by weighting each PET voxel by its tumor membership probability. The goal of the study was to evaluate the relevance of fuzzy-threshold based weighted parameters in prediction of tumor recurrence, in comparison with a “standard” fixed or hard threshold based parameters.

Material and Methods: This study included 53 patients treated for locally advanced cervical cancer by external beam radiation therapy with concurrent chemotheraphy, followed by brachytherapy and ± surgery. All patient underwent 18F-FDG PET/CT exam before the treatment. Different tumor membership probability maps were extracted from 18F-FDG PET images using fuzzy-thresholding defined by a threshold Th and a level of fuzziness ΔTh (both expressed in % of the maximum uptake value) using a Zadeh’s standard function. Fuzzy-thresholding were tested with Th=41%, 50% and 70% and ΔTh from 0% to 40% (ΔTh=0% corresponding to hard-thresholding). Using the fuzzy-thresholding, we computed weighted analogous of four standard 18F-FDG PET parameters; the maximum uptake averaged by its 26 neighbors (SUVpeak), the average SUV inside the tumor region (SUVmean), the metabolic tumor volume (MTV) and the total lesion glycolysis (TLG). The recurrence was defined based on clinical examination, MRI and PET imaging. Median follow-up was 49 months [range: 7-83]. A total of 16 patients developed disease recurrence. The predictive capability of the PET parameters to predict 3 year overall recurrence were evaluated using the area under the receiver operating characteristic curve (AUC) and the p-value of the logistic regression model.

Results: The figure shows the predictive values (AUC and p values) of the weighted parameters depending on the threshold Th and the fuzzy-level Δth used. SUVpeak and SUVmean were not predictive for any of the segmentations tested. TLG and MTV extracted through hard-thresholding (ΔTh=0%) were highly predictive with Th=41% (AUC=0.74, p=0.012) and Th=50% (AUC=0.77, p=0.006) but not with Th=70%. Weighted parameters were discriminative (p=0.05) at Th=41% with Δth = [0% - 22%], at Th=50% with Δth = [0% - 32%] and at Th=70% with Δth = [0% - 32%] indicating a lower sensitivity to the choice of threshold.

Conclusion: PET weighted parameters including voxels tumor membership probability can be used to predict tumor...